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Gauging the proportion and impact of drug-drug interactions in the prescriptions of geriatric patients on medications affecting the cardiovascular system

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ABSTRACT

Cardiovascular ailments belong to some of the most important contributing factors for the mortality and reduction in quality of life in developing nations. Patients on prescriptions with many medications are at a heightened risk for development of adverse reactions especially resulting from drug-drug interactions. This study aimed at assessing the pattern, proportion and impact of such Drug-Drug Interactions (DDIs) in patients with various cardiovascular and non-cardiovascular co-morbidities. This study was conducted in the Department of Internal Medicine of a tertiary care center. Prescription of 200 patients were analysed for demographic information like gender, age, comorbidities and drugs prescribed. DDI were assessed using Micromedex software. This study included 200 prescriptions of people aged 60 years and above. A total of 324 DDIs were identified among which, 24 (7.4%)were major and 127 (39.2)were moderate.The antiplatelet and anticoagulant group of drugs were responsible for majority of DDI, followed by hypertension medications and diabetic medications It can be concluded from this study that the incidence of DDI rises with the rise in number of medications in the prescriptions and there is increase in number of drugs in the prescription with the increase in number of co morbidities.

Keywords: *Cardiovascular Drugs, Drug-Drug Interaction, Major Interaction, Moderate Interactions*

1. INTRODUCTION

Drug-drug interaction (DDI) alludes to adjustment of reaction to one drug by another drug when they are managed at the same time. The adjustment is for the most part quantitative where the reaction is either increased or diminished in intensity but some of the time it is subjective, consequently anomalous or a distinctive sort of reaction is created. The plausibility of DDI emerges at whatever point a patient gets more than one drug and chances increase with number of drugs taken.1 There are various potential DDIs that can result in harmfulness, modification of the required restorative effects and indeed can lead to debilitating condition. Drug-specific variables like dosage, course of administration, drug formulation and the arrangement of drug administration can be determinants of DDI.Poly-Pharmacy (PP) is characterized as concomitant prescription of three or more drugs. 4 PP is common in elderly as they are more often than not having comorbid illnesses. PP and complicated drug regimens utilized for treating the comorbidities in an elderly lead to DDIs and adverse responses. Studies have confirmed this as one of the major hazard components of DDIs. 5 The elderly populace are at increased chance because of diminished working of the systems, more number of solutions due to comorbidities and different drug administrations. Some of the time inappropriate prescribing designs may lead to PP. 6

DDI are classified as7

Contraindicated- drugs contraindicated for concurrent use.
Major- interaction may be life threatening and or require medical intervention to minimize or prevent serious adverse events.
Moderate- interaction may result to exacerbation of patient's condition and or require an alteration in the therapy.
Minor- interaction would have limited clinical effects, may include increase in frequency or severity of side effects but generally would not require major alteration in the therapy.

2. METHODS

In this cross-sectional consider, the information was collected from 200 inpatients aged 60 years or more admitted in Dr. B R Ambedkar Medical College and Hospital, Karnataka, India. Institutional ethics committee approval was obtained. Consider period was from September 2020 to January 2021. This study included all patients aged above 60 years who are on cardiovascular medications. Patient's socioeconomics, pre-existing diseases and drug history were recorded. Drug-Drug interactions were surveyed utilizing Micromedex program on checking on patient's case records. All the quantitative factors like age were communicated as mean and standard deviation. All the qualitative factors were communicated as proportion.In the present study, expecting 95% confidence level 10% relative precision, the study requires a minimum of 181 subjects. Descriptive statistics were analysed and presented in terms of mean, standard deviation and percentage. Chi-square test was used to study the association of age and sex with PP and DDIs. SPSS version 20 was used to analyse the data.

3. RESULTS

A total of 200 prescriptions of elderly patients were analysed. All the quantitative variables like age are indicated as mean and SD. All the qualitative variables are indicated as ratios and proportions. There were 47% (n=94) male and 53% (n=106) female patients in this study (Table 1).

Table 1: Age Distribution

Age (Years)	N (number)
Male	94 (47%)
Female	106 (53%)

Age Distribution Among the 200 prescriptions, 324 interactions were found. The age of this population ranged from 60 to 78 years. The mean age of the patients was 63.19±4.99 years. The number of medications prescribed for a patient ranged from 2 to a maximum of 10 drugs.

The patients were on various groups of drugs acting on the cardiovascular system as follows:

1. Antiplatelet agents- aspirin, clopidogrel,
2. Antihypertensives- CCBs, beta blockers, ACE inhibitors, ARBs, alpha blockers,
3. Electrolytes,
4. Drugs with positive ionotropic effects- digoxin,
5. Anticoagulants.
6. Vasodilators- nitrates, potassium channel activators,
7. Hypolipidemics- statins, fibrates,
8. Diuretics- loop diuretics, thiazides, potassium sparing diuretics, osmotic diuretics,
9. Thyroid and antithyroid agents,

Table 2: Frequency and Effects of DDIs due to CV Drugs

Drugs	Interactions	No. of Patients (n)	Per cent (%)
Aspirin+Clopidogrel	Increases risk of bleeding	27	8.333
Atorvastatin+Clopidogrel	Decreases antiplatelet effect	22	6.790
Aspirin+ Insulin	Increases hypo/hyperglycaemia risk	17	5.246
Aspirin+Furosemide	Decreases diuretic efficacy	14	4.320
Aspirin+Metoprolol	Decreases antihypertensive efficacy	14	4.320
Metoprolol+Insulin	Masks symptoms of hypoglycaemia	13	4.012
Telmisartan+Insulin	Increases risk of hypoglycaemia	11	3.395
Aspirin+Ramipril	Decreases antihypertensive efficacy	10	3.086
Aspirin+Cilostazol	Increases risk of bleeding	9	2.777
Amlodipine+Clopidogrel	Decreases antiplatelet efficacy	9	2.777
Ramipril+Metformin	Increases risk of hypoglycaemia	9	2.777
Aspirin+Enalapril	Decreases antihypertensive efficacy	9	2.777
Ramipril+Spironolactone	Increased risk of hyperkalaemia	6	1.851
Ramipril+Insulin	Increases risk of hypoglycaemia	5	1.543
Insulin+Metformin	Increases risk of hypoglycaemia	4	1.234
Insulin+Levofloxacin	Impaired glycaemic control	3	0.925
Insulin+Losartan	Increases risk of hypoglycaemia	2	0.617
Other combination with cardiovascular drugs with less than or equal to frequency of 4 DDI	with less than or equal to frequency of 4 DDI	140	43.20
Total DDIs	**324**		

Frequency and Effects of DDIs due to CV Drugs On statistical analysis of age of patient and number of drugs by Pearson's Chi Square test, p was significant at less than 0.0001, hence there was statistically significant difference between the age and the number

of drugs in the prescription, and the number of drugs increased with the increase in age. As the age increased the risk of co-morbid illness also increased, so the number of drugs in the prescription also increased. But there was no statistically significant difference in the occurrence of DDI among male and female (p= 0.3). The drugs that were aimed for co-morbid illness like diabetes mellitus, asthma, epilepsy, GERD, peptic ulcers, PVD, acute infections etc. would often interact with different groups of drugs acting on CVS. The interacting drugs belonged to various pharmacological classes like- proton pump inhibitors, H2 blockers, beta agonists, antiepileptics, oral hypoglycemics, insulin, prokinetic agents and antibiotics. It was found that the antiplatelet agent, aspirin was the most common drug to be involved in DDI, followed by insulin. Aspirin would interact with antihypertensives and diuretics and blunt their therapeutic efficacy.

Table 3:

Table 3: Classification of DDIs

Category	n	Percentage (%)
Contra-indicated	2	0.62
Major	24	7.40
Moderate	127	39.20
Minor	189	58.33
Total	324	

4. DISCUSSION

This study involved 200 prescriptions of elderly patients on cardiovascular drugs, of which 106 were females and 94 were males. In this study, the prescription contained minimum of two medications to a maximum of 10 drugs. These prescriptions contained different types of drugs that act on the CVS which belong to the following classes: antihypertensives like ACEIs- enalapril and ramipril, β blockers- atenolol, metoprolol, propranolol, carvedilol and α blockers like prazosin, α agonists- clonidine, moxonidine, diuretics- thiazides, furosemide, torsemide, spironolactone, metolazone, CCBs amlodipine and clinidipine, ARBs- telmisartan, olmesartan and losartan, antiplatelet agents like aspirin, clopidogrel and cilostazol, antianginals like nitrates and drugs like digoxin, ivabradine and ranolazine were used in heart failure. More than 42 pairs of DDI were found. 127 (39.20%) of the DDI were moderate in nature and 24 (7.40%) were major DDI, Table 2 illustrates the effects of these DDI. Antiplatelets were the ones contributing the most for the DDI. In a study conducted by Sharma S et al, a total of 48 DDI was identified in 150 patients. Among them 32 were identified with at least one interacting combination. 20 (65.5%) were identified with single interacting combination, this was followed by the patients who encountered two DDI in 8 (25%) patients and three interactions in 4 (12.5%) pateints.9 Polypharmacy is a major cause of DDI.

According to the analysis of SAGE (Study on global aging) data by Dutta M et al, the prevalence of polypharmacy was 4.2% among elderly in India. This study also showed higher proportion of polypharmacy among male, aged 70-79 years.10 According to Pelliccia F et al study, states that DDI contributed for the inconsistency in the efficacy of clopidogrel to prevent atherothrombotic events.12

According to Corsonello A et al, infections in elderly have increased rate of mortality and morbidity because of the PP regimens which increase the risk of DDI. Additionally, changes in the body composition occurring with advance in age, reduced liver function and perfusion, reduced renal excretion affects the pharmacokinetics and pharmacodynamics.13

5. CONCLUSION

PP increases the hazard of drug-drug interactions, most of these can be reduced with pharmacological alteration of the medication regimen. This too diminishes the rate of antagonistic medicate responses due to drug-drug interactions additionally diminishes the morbidity and mortality. Coordination between the clinician and the clinical pharmacologists plays an fundamental part in individualised and safe medicine.

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